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EXAMINER	
ENEWOLD, J	
ART UNIT	**PAPER NUMBER**
1655	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/241,636	HEATH ET AL.	
	Examiner	Art Unit	
	Jeanine A Enewold	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on *14 January 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☐ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed January 14, 2000. Currently, claims 1-53 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Objections

3. The claims are objected to for the following:

B) Claims 28 and 33-41 are in improper Markush form. (See MPEP 2273.05(h)). A Markush group should read as "...is selected from the group consisting of..."

The objection is maintained because the response makes no remarks on the objection nor obviates the objection.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-25, 45-53 are indefinite because the claims do not recite a positive process step which clearly relates back to the preamble. The preamble states that the method is for "characterizing" DNA but the final process step is purifying DNA. Therefore the claims are unclear as to whether the method is a method of characterizing DNA or purifying DNA.

The response states that purifying DNA is just one step of the overall processing of characterizing DNA. However, the rejection is maintained since characterizing requires more analysis than simply purification. Characterizing generally implies determining some characteristic of the DNA such as size, location within the genome, or function. For the reasons given above and those already on record,,I the rejection is maintained.

B) Claims 1-25 and 45-53 are also indefinite over the recitation in line 1 of claim 1 and 2 of "the step" because this term lacks antecedent basis. This rejection can be overcome by amending to "a step".

The response asserts that the amendment of Claim 1 removes the basis for this rejection, however Claim 1 has not been amended. For the reasons given above and those already on record,, the rejection is maintained.

C) In Claims 4 and 44 are indefinite as it is unclear when the solid support is heated to greater than 60 degrees. That is, as written it is unclear whether the heating occurs after step (a) for the purpose of lysis or after step (c) to achieve release of the DNA from the solid support. Additionally, Claims 4 and 44 are indefinite over the

recitation of "the further step of heating" because "the further step of heating" lacks antecedent basis. Specifically, the claims from which Claims 4 and 44 (claims 1&2 and 26& 27, respectively) depend do not recite "a further step of heating".

The response argues that the steps are not in any order of preference and that the heading of the solid support is a modification of Claim 1 and 2. Moreover, the response argues that the claims do not lack antecedent basis because they are listed as "a further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record,, the rejection is maintained.

D) In Claims 8-10 are indefinite as it is unclear when the counting of the cells should occur in the method and what purpose the counting entails. That is, as written it is unclear whether the counting step occurs before the biological material has been contacted to the solid support or following the contacting with a solid support. Additionally, Claims 8-10 are indefinite over the recitation of "the step of counting" because "the step of counting" lacks antecedent basis. Specifically the claims from which Claims 8-10 depend do not recite "a step of counting".

Although the response amends the claims to clarify that the biological material is from the respective sample, the other rejections were not overcome by this amendment. For the reasons given above and those already on record, the rejection is maintained.

E) Claims 11 and 13 are indefinite over the recitation of "the step of characterizing the remainder of the lysate" because "the remainder", "the step of

characterizing" and "the lysate" lacks antecedent basis. Specifically, the claims from which Claim 11 depends do not recite "a remainder", "a step of characterizing" or a "lysate".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

F) Claims 12 and 14 are indefinite over the recitation of "the step of characterizing the remainder of the biological material" because "the step of characterizing" and "the remainder of the biological material" lacks antecedent basis. Specifically, the claims from which Claim 12 depends do not recite "a step of characterizing" or "a remainder of the biological material".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. That is, the claims are unclear as to what step is being referred to. For the reasons given above and those already on record, the rejection is maintained.

G) Claims 13 and 14 are further indefinite over the recitation of "the step of monitoring impurities" because "the step of monitoring impurities" lacks antecedent basis. Specifically, the claims from which Claim 13 and 14 depend do not recite "a step of monitoring impurities".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

H) Claims 15 and 47 are indefinite over the recitation of "the step of quantitating" because "the step of quantitating" lacks antecedent basis. Specifically, the claims from which Claims 15 and 47 depend do not recite "a step of quantitating".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

I) Claim 16 is indefinite over the recitation of "the step of adjusting the concentration of DNA" because "the step of adjusting the concentration of DNA" lacks antecedent basis. Specifically, the claims from which Claim 16 depends do not recite "a step of adjusting the concentration of DNA".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

J) Claims 17-23 and 48-53 are indefinite over the recitation of "the step of evaluating" because "the step of evaluating" lacks antecedent basis. Specifically, the claims from which Claims 17 and 48 depend do not recite "a step of evaluating".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

K) Claim 18 is further indefinite over the recitation of "the step of determining the yield" because "the step of determining the yield" lacks antecedent basis. Specifically, Claim 17 from which Claim 18 depends, does not recite "a step of determining the yield".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

L) Claims 19 and 49 are indefinite over the recitation of "the step of determining the size" because "the step of determining the size" lacks antecedent basis. Specifically, the claims from which Claims 19 and 49 depend do not recite "a step of determining the size".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to

Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

M) Claim 20 is indefinite over the recitation of "the step of determining the purity" because "the step of determining the purity" lacks antecedent basis. Specifically, the claims from which Claim 20 depends do not recite "a step of determining the purity".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

N) Claims 21 and 50 are indefinite over the recitation of "the step of digesting" because "the step of digesting" lacks antecedent basis. Specifically, the claims from which Claims 21 and 50 depend do not recite "a step of digesting".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

O) Claims 22 and 52 are indefinite over the recitation of "the step of analyzing" because "the step of analyzing" lacks antecedent basis. Specifically, the claims from which Claims 22 and 52 depend do not recite "a step of analyzing".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to

Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

P) Claims 23 and 53 are indefinite over the recitation of "the step of conducting a hybridization analysis" because "the step of conducting a hybridization analysis" lacks antecedent basis. Specifically, the claims from which Claims 23 and 53 depend do not recite "a step of conducting a hybridization analysis".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

Q) Claims 26, 28-41, 44, and 46-53 are indefinite over the recitation of step (a) "contacting....with a solid support treated with a lysing matrix" because this phrase makes the claims unclear as to whether the lysing matrix is a liquid solution which is contacted with a solid support or whether the lysing matrix is the solid support. The specification does not describe contacting a lysis matrix to a solid support but instead describes the lysis matrix as a type of solid support (pg 49, example 24) and teaches contacting lysis reagents (i.e. a solution) to a solid support.

The response asserts that the amendments to the claims remove basis for this rejection, however Claim 26 has not been amended. For the reasons given above and those already on record, the rejection is maintained.

R) Claims 26, 28-41, 44, 46-53 are further indefinite over the recitation of "the lysing reagent" because this term lacks antecedent basis. The claim only recites a "lysing matrix".

The response asserts that the amendments to the claims remove basis for this rejection, however Claim 26 has not been amended. For the reasons given above and those already on record, the rejection is maintained.

T) Claims 24-25 and 45 are indefinite over the recitation of "the step of amplifying" because "the step of amplifying" lacks antecedent basis. Specifically, the claims from which Claims 24-25 and 45 depend, respectively, do not recite "a step of amplifying".

The response asserts that the amendments to the claims remove basis for this rejection, however the claims have not been amended. For the reasons given above and those already on record, the rejection is maintained.

U) Claims 37-41 are indefinite over the recitation of "the lysing reagent" because "the lysing reagent" lacks antecedent basis. Specifically, the claims from which Claims 37-41 depend do not recite "a lysing reagent". Claim 26 only recites a "lysing matrix" and Claim 27 recites no lysing element.

The response asserts that the amendments to the claims remove basis for this rejection, however the claims have not been amended. For the reasons given above and those already on record, the rejection is maintained.

V) Claim 51 is indefinite over the recitation of "the step of sequencing" because "the step of sequencing" lacks antecedent basis. Specifically, the claims from which Claim 51 depends do not recite "a step of sequencing".

The response argues that since the claims lack antecedent basis they are listed as a "further step...". However, despite the fact that the claims list a further step to Claims 1 and 2, they must still have proper antecedent basis. For the reasons given above and those already on record, the rejection is maintained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 5-6, 8, 11-21, 23-30, 32-33, 37, 39, 41, 45-51, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Boom et al (5,234,809).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59).

The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the remainder of the biological matter is purified (washing buffer, alcohol washing solution and acetone.) Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50)(limitations of claims 24-27 and 45-46). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. As described in Boom, the DNA may be eluted from the solid support by means of an eluting reagent (col.4, line 33). Boom teaches an eluting reagent can be TE buffer, aqua bidest or PCR buffer. Boom further teaches the process where in the solid support is contained in a single vessel (col.4, lines 34-36) (limitations of claims 3 and 28). Boom demonstrates the use of isolating nucleic acids from a nucleic acid-containing biological material (col. 1, lines 10-20). The biological material stated includes tissues, cell cultures, blood, urine, and saliva (body fluids)(limitations of claims 5-6, 29-30). The nucleic acid was taught to be examined by gel electrophoresis (col. 10, lines 13-24) (limitations of claims 12-17, 19, 21, 47-49). This method may be used for characterizing the biological material and monitoring impurities. Yields were also taught in example A1 (col. 12, lines 46-48)(limitations of claim 18). Eluted DNA was treated with a restriction

enzyme, electrophoresed and visualized (col 12 65-68) (limitations of claims 21 and 50). Boom also teaches hybridization analysis of the isolated nucleic acids (col. 9, lines 19-21)(limitations of claims 23 and 53). Boom teaches a method which can "provide a process with which nucleic acid can be isolated immediately (without pretreatments) ..." (col. 1, lines 64-67) (limitation of claim 32). Boom teaches lysis buffers containing Tris (buffer), aqua bidest, GuSCN, and EDTA (col 6, lines 39-68). Therefore, since Boom has taught a method having every limitation recited in the claimed methods Boom reads on the claimed method.

Response to Arguments

Applicant traversed this rejection on the following grounds. The response argues that Boom's method mixes the nucleic acid-containing starting material, a chaotrophic substance, and a nucleic acid binding phase together to form a particulate suspension and also that Boom uses chaotrophic substances which are harsh substances, unlike the instant invention. This argument has been reviewed but is not convincing because the instant claims are not drawn to a method which recites the use of a lysing reagent which is composed of detergent effective to lyse cells or protein coats sufficiently to release DNA; water, and optionally, a chelating agent to reduce DNA damage, and a buffer effective to provide a pH of greater than about 2. Instead the claims broadly encompass a method of characterizing DNA comprising the steps of isolating nucleic acids by contacting a biological material that contains DNA with a solid support treated with a lysing reagent; treating the biological material that contains DNA with a DNA

purifying reagent; and purifying the DNA from the remainder of the biological material. There is no step in the claims which excludes the use of a harsh lysing reagent (chaotrophic substance) as the lysing reagent. A lysing reagent, as recited in the claims, is a broad term that may include any reagent which causes lysis including chaotrophic substances and detergents.

The response also argues that Boom's method differs from their method in that the current invention "recites the use of a solid support to which the lysing reagent is added, and the excess lysis reagent removed". However, these limitations are not limitations of the claims. Moreover, the claims do not recite the solid supprot to which the lysis reagent is added is then dried. Boom's method does not teach the drying of a lysing reagent to a solid support. However, the recitation of the claims is "contacting a biological material that contains DNA with a solid support treated with a lysing reagent" which is clearly encompassed by the method of Boom which adds lysing reagent (chaotropic substances) to a vessel containing a solid support and subsequently adding the biological material (col. 4, lines 9-12).

It is noted that the rejections of the independent Claims 2, 26 and 27 were not addressed in the response. Therefore, for these reasons and those already of record, the rejection is maintained.

7. Claims 1-20, 24-33, 37-41, and 44-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Deggerdal (WO 96/18731).

Deggerdal teaches methods of characterizing DNA. Deggerdal discloses a "method of isolating nucleic acid from a sample, said method comprising contacting said sample with a detergent and a solid support, whereby soluble nucleic acid in said sample is bound to the support, and separating said support with bound nucleic acid from the sample" (pg 5, para 2). Deggerdal teaches that the "nucleic acid-containing sample may be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. The solid support was contained in a vessel (pg 26, line 18). Deggerdal teaches isolation of nucleic acids and the elution of the nucleic acid by heating to 65 C for 5-10 minutes (pg 12, para 3, line 3)(limitations of claims 4 and 44). The samples may be of "any material containing nucleic acid" (pg 6, para 1, line 1-3)(limitations of claims 5-7 and 29-31). Deggerdal teaches a method of DNA isolation from cultured cells which indicates the number of cells used as starting material (pg 33, line 1) (limitations of claims 8-10). The purified DNA was then analyzed by PCR and visualized on agarose gel electrophoresis (pg 20, lines 29-32). Detection of extra bands indicated contamination (pg 17, lines 26-27). The solid support was taught to be made of "glass, silica, latex or a polymeric material" (pg 9, para 3)(limitations of claim 33). Deggerdal teaches an example where cells were lysed using DNA DIRECT Dynabeads and the lysate from each sample was

further characterized (pg 35, lines 6-35)(limitations of claim 11). Deggerdal teaches the lysing reagent as a detergent. This detergent may be supplied in simple aqueous solution (pg 8, line 7). Further any suitable buffer (Tris) is taught. The reagent may also include components such as enzymes, chelating agents and reducing agents (pg 8, lines 7-23) (limitations of claims 37-41). Therefore, since Deggerdal has taught a method having every limitation recited in the claimed methods, Deggerdal reads on the claimed method.

Response to Arguments

Applicant traversed this rejection on the following grounds. The response argues that Deggerdal's method teaches "a method of isolating nucleic acids from a samle, said method comprising contacting said sample with a detergent and a solid support...", thus Deggerdal does not teach pre-treating the solid support with a lysing reagent prior to contacting it with the biological material. However, the Deggerdal teaches in the specification that the "nucleic acid-containing sample may be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Thus Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound" with the recitation that the sample may be added subsequently to the detergent.

It is noted that the rejections of the independent Claims 2, 26 and 27 were not addressed in the response. Therefore, for these reasons and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Deggerdal (WO 96/18731).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59).

The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the remainder of the biological matter is purified (washing buffer, alcohol washing solution and acetone.) Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support.

Boom does not teach a lysing reagent which does not contain a buffer.

Deggerdal, however, teaches a lysing reagent as a detergent. This detergent may be supplied in simple aqueous solution (pg 8, line 7). Further any suitable buffer (Tris) is taught. The reagent may also include components such as enzymes, chelating agents and reducing agents (pg 8, lines 7-23) (limitations of claims 37-41).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have modified the method of Boom to include the use of the lysing reagents taught in Deggerdal. The ordinary artisan would have been motivated to use the lysing reagents taught in Deggerdal because the lysing reagents taught in Deggerdal were readily available.

Response to Arguments

Applicant traversed this rejection on the following grounds. The response argues that Boom's method mixes the nucleic acid-containing starting material, a chaotrophic substance, and a nucleic acid binding phase together to form a particulate suspension and also that Boom uses chaotrophic substances which are harsh substances, unlike the instant invention. This argument has been reviewed but is not convincing because the instant claims are not drawn to a method which recites the use of a lysing reagent which is composed of detergent effective to lyse cells or protein coats sufficiently to release DNA; water, and optionally, a chelating agent to reduce DNA damage, and a buffer effective to provide a pH of greater than about 2. Instead the claims broadly encompass a method of characterizing DNA comprising the steps of isolating nucleic acids by contacting a biological material that contains DNA with a solid support treated with a lysing reagent; treating the biological material that contains DNA with a DNA purifying reagent; and purifying the DNA from the remainder of the biological material. There is no step in the claims which excludes the use of a harsh lysing reagent (chaotrophic substance) as the lysing reagent. A lysing reagent, as recited in the claims, is a broad term that may include any reagent which causes lysis including chaotrophic substances and detergents.

The response also argues that Boom's method differs from their method in that the current invention "recites the use of a solid support to which the lysing reagent is added, and the excess lysis reagent removed". However, these limitations are not

limitations of the claims. Moreover, the claims do not recite the solid supprot to which the lysis reagent is added is then dried. Boom's method does not teach the drying of a lysing reagent to a solid support. However, the recitation of the claims is "contacting a biological material that contains DNA with a solid support treated with a lysing reagent" which is clearly encompassed by the method of Boom which adds lysing reagent (chaotropic substances) to a vessel containing a solid support and subsequently adding the biological material (col. 4, lines 9-12).

The response also argues that Deggerdal's method teaches "a method of isolating nucleic acids from a sample, said method comprising contacting said sample with a detergent and a solid support...", thus Deggerdal does not teach pre-treating the solid support with a lysing reagent prior to contacting it with the biological material. However, Deggerdal, in the specification, expands further and discloses that the "nucleic acid-containing sample may be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Thus Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound" with the recitation that the sample may be added subsequently to the detergent (col. 4, lines 9-12).

Therefore, for these reasons and those already of record, the rejection is maintained.

10. Claims 23 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deggerdal (WO 96/18731) in view of Boom (5,234,809).

Deggerdal teaches methods of characterizing DNA. Deggerdal discloses a "method of isolating nucleic acid from a sample, said method comprising contacting said sample with a detergent and a solid support, whereby soluble nucleic acid in said sample is bound to the support, and separating said support with bound nucleic acid from the sample" (pg 5, para 2). Deggerdal teaches that the "nucleic acid-containing sample may....be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. The solid support was contained in a vessel (pg 26, line 18). Deggerdal teaches isolation of nucleic acids and the elution of the nucleic acid by heating to 65 C for 5-10 minutes (pg 12, para 3, line 3)(limitations of claims 4 and 44). The samples may be of "any material containing nucleic acid" (pg 6, para 1, line 1-3)(limitations of claims 5-7). Deggerdal teaches a method of DNA isolation from cultured cells which indicates the number of cells used as starting material (pg 33, line 1) (limitations of claims 8-9). The purified DNA was then analyzed by PCR and visualized on agarose gel electrophoresis (pg 20, lines 29-32).

Deggerdal does not teach conducting a hybridization analysis on the amplified DNA.

Boom teaches hybridization analysis of the isolated nucleic acids (col. 9, lines 19-21).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have applied the method of Deggerdal to include the method of hybridization reactions as used in the method of Boom. The ordinary artisan would have been motivated to have conducted hybridization reactions taught in the method of Boom on the isolated DNA obtained from the Deggerdal method to further characterize the DNA sample.

Response to Arguments

The response traversed the rejection on the same grounds as given above. Discussions can be found above which describe the reasons why the rejections of Boom and Deggerdal are appropriate are also appropriate in response to Deggerdal and Boom.

Therefore, for these reasons and those already of record, the rejection is maintained.

11. Claims 7, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,234,809) in view of Su (5,804,684).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59). The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the remainder of the biological matter is purified (washing buffer, alcohol washing solution and acetone.) Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support.

Boom does not specifically teach biological material from the group consisting of environmental samples taken from air, water, sediment and soil. Although Boom teaches that a variety of solid support can be used (col. 2, lines 52-63), he does not specifically teach the solid support recited in the claims.

However, Su teaches a list of samples which includes "any type of biological sample....environmental, nutritional, scientific or industrial significance" (col.8, lines 3-16).

Su teaches the use of cellulose, rayon, cellulose acetate, silica and more as suitable solid supports for DNA isolation (col.3, lines 35-49; col 15, line 18).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have applied the method of Boom to include the use of environmental samples as the biological starting material as used in the method of Su. The ordinary artisan would have been motivated to have sampled the biological materials from the environment because environmental samples are a well known source of clinically important DNA containing organisms whose detection is necessary to prevent disease spread, for example.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have applied the method of Boom to include the use of other solid supports as used in the method of Su. Also, the ordinary artisan would have suspected that using the methods described in Boom with solid supports other than silica beads would provide similar results because Su teaches the use of polysaccharides, protein/polypeptides, synthetic fibers, synthetic plastics and silica are all suitable solid supports.

Response to Arguments

The response traversed the rejection on the same grounds as given above. Discussions can be found above which describe the reasons why the rejections of Boom and Deggerdal are appropriate.

Therefore, for these reasons and those already of record, the rejection is maintained.

12. Claims 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5, 804,684) or Deggerdal (WO 96/18731) in view of Su (5,804684).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59). The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the remainder of the biological matter is purified (washing buffer, alcohol washing solution and acetone.) Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support.

Deggerdal teaches methods of characterizing DNA. Deggerdal discloses a "method of isolating nucleic acid from a sample, said method comprising contacting said

sample with a detergent and a solid support, whereby soluble nucleic acid in said sample is bound to the support, and separating said support with bound nucleic acid from the sample" (pg 5, para 2). Deggerdal teaches that the "nucleic acid-containing sample may....be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. The solid support was contained in a vessel (pg 26, line 18). Deggerdal teaches isolation of nucleic acids and the elution of the nucleic acid by heating to 65 C for 5-10 minutes (pg 12, para 3, line 3)(limitations of claims 4 and 44). The samples may be of "any material containing nucleic acid" (pg 6, para 1, line 1-3)(limitations of claims 5-7). Deggerdal teaches a method of DNA isolation from cultured cells which indicates the number of cells used as starting material (pg 33, line 1) (limitations of claims 8-9). The purified DNA was then analyzed by PCR and visualized on agarose gel electrophoresis (pg 20, lines 29-32).

Boom nor Deggerdal not teach the eluting reagent as specified in the claims..

Su teaches the elution buffer to be 5 mM Tris HCl, pH 9, and 0.5 mM EDTA (col 10, line 17).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have modified the method of Boom or Deggerdal to

include the use of the elution buffer described in the method of Su. The ordinary artisan would also have expected that using the elution buffer of Su in the method of Boom or Deggerdal with the elution buffer described in Su would have provided equivalent results.

Response to Arguments

The response traversed the rejection on the same grounds as given above. Discussions can be found above which describe the reasons why the rejections of Boom and Deggerdal are appropriate.

Therefore, for these reasons and those already of record, the rejection is maintained.

13. Claims 22 and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) or Deggerdal (WO 96/18731) in view of Sambrook (Molecular Cloning).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59). The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the remainder of the biological matter is purified (washing buffer, alcohol washing solution

and acetone.) Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support.

Deggerdal teaches methods of characterizing DNA. Deggerdal discloses a "method of isolating nucleic acid from a sample, said method comprising contacting said sample with a detergent and a solid support, wherby soluble nucleic acid in said sample is bound to the support, and separating said support with bound nucleic acid from the sample" (pg 5, para 2). Deggerdal teaches that the "nucleic acid-containing sample may....be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. The solid support was contained in a vessel (pg 26, line 18). Deggerdal teaches isolation of nucleic acids and the elution of the nucleic acid by heating to 65 C for 5-10 minutes (pg 12, para 3, line 3)(limitations of claims 4 and 44). The samples may be of "any material containing nucleic acid" (pg 6, para 1, line 1-3)(limitations of claims 5-7). Deggerdal

teaches a method of DNA isolation from cultured cells which indicates the number of cells used as starting material (pg 33, line 1) (limitations of claims 8-9). The purified DNA was then analyzed by PCR and visualized on agarose gel electrophoresis (pg 20, lines 29-32).

Boom nor Deggerdal specifically teach sequencing the purified DNA.

However, Sambrook teaches the analysis of DNA by nucleic acid sequencing (13.3). Sambrook teaches that the sequences provide the advantage of determining the sequence of nucleotides in a particular DNA molecule.

Therefore, it would have been prima facie obvious to one of ordinary shill at the time of the invention was made to have modified the method of Boom or Deggerdal to include the sequencing analysis method taught by Sambrook in order to make the claimed invention as a while. The ordinary artisan would be motivated to have sequenced the purified DNA obtained by the Boom method in order to have achieved the expected advantage of determining the sequence of nucleotides of the isolated DNA.

Response to Arguments

The response traversed the rejection on the same grounds as given above. Discussions can be found above which describe the reasons why the rejections of Boom and Deggerdal are appropriate.

Therefore, for these reasons and those already of record, the rejection is maintained.

14. Claims 33 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom (5,804,684) or Deggerdal (WO 96/18731) in view of Arnold (5,599,667).

Boom teaches methods of characterizing DNA. Boom discloses a process which involved contacting the biological material that contains DNA with a solid support that had been treated with a lysing reagent (i.e. a chaotropic substance), treating the biological material with a purifying reagent, and purifying the DNA (col. 4, lines 3-59). The chaotropic substance (lysing reagent) is contacted with silica particles (solid support). The biological material is then treated with purifying reagents, and the remainder of the biological matter is purified (washing buffer, alcohol washing solution and acetone.) Additionally, the process described by Boom produces DNA which can be further used to "demonstrate NA sequences by means of an amplification method such as the PCR method...." (col.4, lines 48-50). Since Boom teaches that the Gus SCN (i.e. the lysis reagent) is added to the solid support (i.e. the silica beads) prior to addition of biological material, Boom is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support.

Deggerdal teaches methods of characterizing DNA. Deggerdal discloses a "method of isolating nucleic acid from a sample, said method comprising contacting said sample with a detergent and a solid support, wherby soluble nucleic acid in said sample is bound to the support, and separating said support with bound nucleic acid from the

sample" (pg 5, para 2). Deggerdal teaches that the "nucleic acid-containing sample may....be contacted with the detergent and solid phase which may be added to the sample prior to, simultaneously with, or subsequently to the detergent (which functions in the method to lyse)"(pg 7, para 3, lines 22-29). Deggerdal is inherently teaching a solid support to which a lysing reagent is "bound." The term "bound" is being broadly interpreted to mean loosely and transiently in contact with the solid support. The solid support was contained in a vessel (pg 26, line 18). Deggerdal teaches isolation of nucleic acids and the elution of the nucleic acid by heating to 65 C for 5-10 minutes (pg 12, para 3, line 3)(limitations of claims 4 and 44). The samples may be of "any material containing nucleic acid" (pg 6, para 1, line 1-3)(limitations of claims 5-7). Deggerdal teaches a method of DNA isolation from cultured cells which indicates the number of cells used as starting material (pg 33, line 1) (limitations of claims 8-9). The purified DNA was then analyzed by PCR and visualized on agarose gel electrophoresis (pg 20, lines 29-32).

Boom nor Deggerdal specifically teach using polyolefin as a solid support wherein polyolefin is hydrophilic and has a charge.

However, Arnold teaches polycationic solid supports that can be used purification of nucleic acids (see abstract). The polycationic support matrix is taught to include inorganic and organic materials which include glasses, polyolefins and polysaccharides (col.8, lines 55-62).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time of the invention was made to have modified the method of Boom or Deggerdal to include the solid supports of Arnold in order to make the claimed invention as a whole. The ordinary artisan would be motivated to have substituted polyolefins as a solid support in the Boom or Deggerdal method because Arnold taught that polyolefins and glass are both suitable for DNA isolation because they meet the same "principle requirement" of "not unduly adsorbing either contaminants or nucleotide probes (col. 8, lines 61-64). Consequently Arnold shows that the silica of Boom or Deggerdal and the polyolefins of the claims are equivalent.

Response to Arguments

The response traversed the rejection on the same grounds as given above. Discussions can be found above which describe the reasons why the rejections of Boom and Deggerdal are appropriate. Moreover, the solid supports of Arnold are solid supports which may be used for characterizing DNA. The claims do not include the recitation that the detergent molecules are bound to the solid support.

Therefore, for these reasons and those already of record, the rejection is maintained.

15. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al (5,234,809) or Deggerdal (WO 96/17831) in view of Arnold (5,599,6667) as applied to claim 33, 35-36 above, and further in view of Hasebe (5,151,345).

Arnold teaches polycationic solid supports that can be used purification of nucleic acids (see abstract). The polycationic support matrix is taught to include inorganic and organic materials which include glasses, polyolefins and polysaccharides (col.8, lines 55-62).

However, neither Boom or Deggerdal nor Arnold specifically teaches that polyolefin is a mixture of low density polyethylene and polypropylene fibers.

However, Hasebe teaches that "a polyolefin resin is preferred, and low-density polyethylene, high-density polyethylene...or a blend thereof is preferably used"(col 11, lines 32-39).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to combine the methods of Boom or Deggerdal and Arnold as discussed above and use the types of polyolefins taught by Hasebe. As Arnold teaches that "polyolefins" may be used in DNA isolation, one of ordinary skill in the art would have been motivated to use a preferred polyolefin resin.

Response to Arguments

The response traversed the rejection on the same grounds as given above. Discussions can be found above which describe the reasons why the rejections of Boom and Deggerdal are appropriate.

Therefore, for these reasons and those already of record, the rejection is maintained.

New Grounds for Objection necessitated by Amendment

16. Claims 4 and 5 are objected to over the recitation "the process according to claims or 2". The claim seems to omit the number 1 following the word "claims". It is presumed the claim should read "the process according to claims **1** or 2". Similarly, it is presumed that Claim 5 omitted the number **2** following the word "or".

Conclusion

17. **No Claims are allowable over the prior art.**

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to. 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 308- 4242.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Enewold
February 23, 2000

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP ~~1800~~ 1600